

INTERNATIONAL COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

PETT, Christopher, Phineas
Frank B. Dehn & Co.
179 Queen Victoria Street
London EC4V 4EL
ROYAUME-UNI

Date of mailing (day/month/year) 30 January 2001 (30.01.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 86.61.70445/002	
International application No. PCT/GB00/00644	International filing date (day/month/year) 23 February 2000 (23.02.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address GUSTOW, Evan P.O. Box 363 Ardmore, PA 19003 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address GUSTOW, Evan 626 Conestoga Road Villanova PA 19085 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Lazar Joseph Panakal Telephone No.: (41-22) 338.83.38
---	--

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 86.61.70445/002	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 00644	International filing date (day/month/year) 23/02/2000	(Earliest) Priority Date (day/month/year) 11/06/1999
Applicant NYCOMED AMERSHAM PLC et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00644

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/10 G21G4/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N G21G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 994 013 A (SUTHANTHIRAN KRISHNAN ET AL) 19 February 1991 (1991-02-19) the whole document	1,2,4-6, 8-11,13
Y	-----	7,12,14
Y	US 4 550 100 A (HOFMEISTER HELMUT ET AL) 29 October 1985 (1985-10-29) column 2, line 16 - line 24 column 3, line 32 - line 59	7,12
Y	-----	
Y	US 5 199 939 A (DAKE MICHAEL D ET AL) 6 April 1993 (1993-04-06) abstract	14
A	-----	
	US 5 342 283 A (GOOD ROGER R) 30 August 1994 (1994-08-30) column 4, line 10 - line 15 column 6, line 3 - line 21	3-6,15
	----- -/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

2 June 2000

Date of mailing of the international search report

13/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Capostagno, E

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/00644

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 19713 A (STS BIOPOLYMERS INC ;VIOLANTE MICHAEL R PH D (US); LYDON MARGARET) 14 May 1998 (1998-05-14) page 2, line 28 -page 3, line 24 -----	3,15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00644

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4994013	A	19-02-1991	US 5163896 A	17-11-1992
US 4550100	A	29-10-1985	DE 3242892 C	12-07-1984
			AT 38235 T	15-11-1988
			DE 3378317 D	01-12-1988
			EP 0113812 A	25-07-1984
			JP 59152400 A	31-08-1984
US 5199939	A	06-04-1993	NONE	
US 5342283	A	30-08-1994	AT 177018 T	15-03-1999
			AU 8920791 A	17-03-1992
			CA 2067804 A	14-02-1992
			DE 69130944 D	08-04-1999
			DE 69130944 T	01-07-1999
			EP 0500928 A	02-09-1992
			JP 5503303 T	03-06-1993
			WO 9203179 A	05-03-1992
WO 9819713	A	14-05-1998	AU 5146098 A	29-05-1998
			CN 1236322 A	24-11-1999
			EP 0941128 A	15-09-1999

PCT

REC'D 17 SEP 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NIDN 73247-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00644	International filing date (day/month/year) 23/02/2000	Priority date (day/month/year) 11/06/1999
International Patent Classification (IPC) or national classification and IPC A61N5/10		
Applicant NYCOMED AMERSHAM PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18/12/2000	Date of completion of this report 13.09.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bichlmayer, K-P Telephone No. +49 89 2399 2977 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00644

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-30 as originally filed

Claims, No.:

1-7,14,15 as originally filed

8-13 as received on 31/05/2001 with letter of 31/05/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00644

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13-14.

because:

☒ the said international application, or the said claims Nos. 13-14 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-10,12,15
 No: Claims 11

Inventive step (IS) Yes: Claims

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00644

	No:	Claims	1-10,12,15
Industrial applicability (IA)	Yes:	Claims	1-12,15
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

Ad section III:

Claims 13 and 14 concern a method of treatment of the human or animal body by therapy (and surgery) for which the International Examination Authority is not required to perform an international preliminary examination (Rule 67.1 iv PCT).

Ad section V:

Reference is made to the following documents:

D1: US,A,3 351 049 (cited in the application)

D2: US,A,4 994 013

D3: US,A,4 323 055 (cited in the application)

1) Independent claim 1

D1 discloses a therapeutic metal seed containing within a radioactive isotope disposed on a carrier. As can be taken from the description on col. 3, line 30, **radioisotope iodine-125** is adsorbed (cf. on col. 5, lines 27 to 33) on a carrier body which is constructed of a material of low-atomic number elements so as to minimize internal absorption of the X-ray radiations, such as nylon (cf. example on col. 7). Thus, the subject-matter of the independent claim 1 is distinguished over D1 in that **iodide-125** or an **iodine-containing compound** are used as source of radioactivity rather than **molecular radioactive iodine-125**. The mere replacement of molecular iodine-125 by its equivalents **iodide-125** or an **iodine-containing compound** is considered to be obvious with respect to D2 and D3, respectively, which discloses sodium iodide (radioisotope) impregnated on (i. e. adsorbed) carbon (D2: cf. on col. 2, lines 40 to 60) which covers a metal substrate.

For this reason, the subject-matter of claim 1 lacks an inventive step, contrary to the requirements of Art. 33(3) PCT. This applies also when considering D3 as the closest prior art which is distinguished from claim 1 only by the feature that the substrate is substantially non-radiation

attenuating since this feature is already known from D1 providing the advantage of enhancing the amount of radiation available.

2) Dependent claims 2 to 10

The features of the dependent claims 2 to 10 are either known from D2 (cf. col. 5, lines 10 to 25; col. 8, lines 29 to 34; example 1) or from D1 (example on col. 7) such that these claims also lack an inventive step (Art. 33(3) PCT).

3) Independent claims 11 and 12

The subject-matter of the independent claim 11 is considered to be known from D2 which discloses adsorbing of a solution of I-125 NaJ on carbon-coated (i.e. substrate) pellets (cf. example 2). Thus, independent claim 11 does not meet the requirements set out in Art. 33(2) PCT.

Starting from D2 the skilled person would consider a radioactive iodine-containing compound when looking for an alternative source of iodine radioisotopes to be adsorbed onto carbon. Thus, the independent claim 12 lacks an inventive step, contrary to the requirements of Art. 33(3) PCT.

4) Independent claim 15

D1 specifically discloses a radioactive source comprising a nylon filament having adsorbed thereon iodine-125 and being mounted into a stainless steel container which at the end is completely sealed. Although D1 does not explicitly mention that said container is echogenic, the skilled man knows that many metals (for example stainless steel or titanium used in D1) are echogenic. Consequently, echogenicity would be detectable and therefore, this feature is considered inherently disclosed by D1. Thus, the subject-matter of claim 15 is distinguished from D1 in that radioactive isotopes of **iodide ions** or an **iodine-containing compound** is adsorbed on the substrate rather than molecular radioactive iodine. The mere replacement of free radioactive iodine by a radioactive isotope of iodide ions cannot be regarded as providing an inventive step with respect to D2 and D3 which

teach that also other forms of radioactive iodine (for example iodide ions) can be used in manufacturing a radioactive source. Thus, claim 15 does not provide an inventive step within the sense of Art. 33(3) PCT.

Ad section VII:

- 1) Independent claims 1 and 15 are not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).
- 2) Incorporation by reference (cf. at page 11) may not be accepted by some of the contracting states.

PATENT COOPERATION TREATY

RECEIVED

17 SEP 2001

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

CANNING, Lewis Reuben et al.
NYCOMED AMERSHAM PLC
Amersham Laboratories
White Lion Road
Amersham
Buckinghamshire HP7 9LL
GRANDE BRETAGNE

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year) 13.09.2001

Applicant's or agent's file reference
NIDN 73247-PCT

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/00644

International filing date (day/month/year)
23/02/2000

Priority date (day/month/year)
11/06/1999

Applicant
NYCOMED AMERSHAM PLC et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

DUE DATE:	17/9/01
FORMALITIES:	SH ✓
PAT. OFF:	LRC ✓
ON DB:	19/9/01
CASE NO:	73247-WO

ON XL
ON DB

Name and mailing address of the IPEA/

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Marra, E

Tel. +49 89 2399-7235



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NIDN 73247-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00644	International filing date (day/month/year) 23/02/2000	Priority date (day/month/year) 11/06/1999
International Patent Classification (IPC) or national classification and IPC A61N5/10		
Applicant NYCOMED AMERSHAM PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18/12/2000	Date of completion of this report 13.09.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bichlmayer, K-P Telephone No. +49 89 2399 2977 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00644

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-30 as originally filed

Claims, No.:

1-7,14,15 as originally filed

8-13 as received on 31/05/2001 with letter of 31/05/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00644

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13-14.

because:

☒ the said international application, or the said claims Nos. 13-14 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-10,12,15

No: Claims 11

Inventive step (IS) Yes: Claims

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00644

	No:	Claims	1-10,12,15
Industrial applicability (IA)	Yes:	Claims	1-12,15
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/00644

Ad section III:

Claims 13 and 14 concern a method of treatment of the human or animal body by therapy (and surgery) for which the International Examination Authority is not required to perform an international preliminary examination (Rule 67.1 iv PCT).

Ad section V:

Reference is made to the following documents:

D1: US,A,3 351 049 (cited in the application)

D2: US,A,4 994 013

D3: US,A,4 323 055 (cited in the application)

1) Independent claim 1

D1 discloses a therapeutic metal seed containing within a radioactive isotope disposed on a carrier. As can be taken from the description on col. 3, line 30, **radioisotope iodine-125** is adsorbed (cf. on col. 5, lines 27 to 33) on a carrier body which is constructed of a material of low-atomic number elements so as to minimize internal absorption of the X-ray radiations, such as nylon (cf. example on col. 7). Thus, the subject-matter of the independent claim 1 is distinguished over D1 in that **iodide-125** or an **iodine-containing compound** are used as source of radioactivity rather than **molecular radioactive iodine-125**. The mere replacement of molecular iodine-125 by its equivalents **iodide-125** or an **iodine-containing compound** is considered to be obvious with respect to D2 and D3, respectively, which discloses sodium iodide (radioisotope) impregnated on (i. e. adsorbed) carbon (D2: cf. on col. 2, lines 40 to 60) which covers a metal substrate.

For this reason, the subject-matter of claim 1 lacks an inventive step, contrary to the requirements of Art. 33(3) PCT. This applies also when considering D3 as the closest prior art which is distinguished from claim 1 only by the feature that the substrate is substantially non-radiation

attenuating since this feature is already known from D1 providing the advantage of enhancing the amount of radiation available.

2) Dependent claims 2 to 10

The features of the dependent claims 2 to 10 are either known from D2 (cf. col. 5, lines 10 to 25; col. 8, lines 29 to 34; example 1) or from D1 (example on col. 7) such that these claims also lack an inventive step (Art. 33(3) PCT).

3) Independent claims 11 and 12

The subject-matter of the independent claim 11 is considered to be known from D2 which discloses adsorbing of a solution of I-125 NaJ on carbon-coated (i.e. substrate) pellets (cf. example 2). Thus, independent claim 11 does not meet the requirements set out in Art. 33(2) PCT.

Starting from D2 the skilled person would consider a radioactive iodine-containing compound when looking for an alternative source of iodine radioisotopes to be adsorbed onto carbon. Thus, the independent claim 12 lacks an inventive step, contrary to the requirements of Art. 33(3) PCT.

4) Independent claim 15

D1 specifically discloses a radioactive source comprising a nylon filament having adsorbed thereon iodine-125 and being mounted into a stainless steel container which at the end is completely sealed. Although D1 does not explicitly mention that said container is echogenic; the skilled man knows that many metals (for example stainless steel or titanium used in D1) are echogenic. Consequently, echogenicity would be detectable and therefore, this feature is considered inherently disclosed by D1. Thus, the subject-matter of claim 15 is distinguished from D1 in that radioactive isotopes of **iodide ions** or an **iodine-containing compound** is adsorbed on the substrate rather than molecular radioactive iodine. The mere replacement of free radioactive iodine by a radioactive isotope of iodide ions cannot be regarded as providing an inventive step with respect to D2 and D3 which

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International application No. PCT/GB00/00644

teach that also other forms of radioactive iodine (for example iodide ions) can be used in manufacturing a radioactive source. Thus, claim 15 does not provide an inventive step within the sense of Art. 33(3) PCT.

Ad section VII:

- 1) Independent claims 1 and 15 are not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).
- 2) Incorporation by reference (cf. at page 11) may not be accepted by some of the contracting states.

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8. A radioactive source as claimed in any of claims 1 to 7 wherein the substrate is carbon, alumina, a zeolite, a titanium oxide, silica, a silicon oxide, a zeolite-type trivalent metal silicate, a metal phosphate, a metal hydroxyphosphate, a glassy material, aluminium nitride, a ceramic, a radiation resistant polymer, bone, coral, coal, limestone, cellulose, starch, agar, gelatin, chitin or hair.
9. A radioactive source as claimed in any of claims 1 to 7 wherein the substrate is carbon.
10. A radioactive source as claimed in any one of claims 1 to 9 which further comprises a binder.
11. A method for the preparation of a radioactive substrate suitable for use in a brachytherapy source, the method comprising exposing a substantially non-radiation attenuating substrate other than ion-exchange resin to a source of radioactive iodide ions with the result that the iodide ions are adsorbed onto the surface of the substrate.
12. A method for the preparation of a radioactive substrate suitable for use in a brachytherapy source, the method comprising exposing a substantially non-radiation attenuating substrate to a radioactive iodine-containing compound with the result that the iodine-containing compound is absorbed onto the surface of the substrate.
13. A method of treatment of a condition which is responsive to radiation therapy which comprises the temporary placement of a radioactive source comprising a radioisotope of iodine in the form of iodide ions or an iodine-containing compound adsorbed on the surface of a substantially non-radiation attenuating substrate at the site to be treated within a patient for a sufficient

8. A radioactive source as claimed in any of claims 1 to 7 wherein the substrate is carbon, alumina, a zeolite, a titanium oxide, silica, a silicon oxide, a zeolite-type trivalent metal silicate, a metal phosphate, a metal hydroxyphosphate, a glassy material, aluminium nitride, a ceramic, a radiation resistant polymer, bone, coral, coal, limestone, cellulose, starch, agar, gelatin, chitin or hair.
- 10 9. A radioactive source as claimed in any of claims 1 to 7 wherein the substrate is carbon.
10. A radioactive source as claimed in any one of claims 1 to 9 which further comprises a binder.
- 15 11. A method for the preparation of a radioactive substrate suitable for use in a brachytherapy source, the method comprising exposing a substantially non-radiation attenuating substrate other than ion-exchange resin to a source of radioactive iodide ions such that the iodide ions are adsorbed onto the surface of the substrate.
- 20 12. A method for the preparation of a radioactive substrate suitable for use in a brachytherapy source, the method comprising exposing a substantially non-radiation attenuating substrate to a radioactive iodine-containing compound such that the iodine-containing compound is absorbed onto the surface of the substrate.
- 25 13. A method of treatment of a condition which is responsive to radiation therapy which comprises the temporary placement of a radioactive source comprising a radioisotope of iodine in the form of iodide ions or an iodine-containing compound adsorbed on the surface of a substantially non-radiation attenuating substrate at the site to be treated within a patient for a sufficient
- 35

INTERNATIONAL SEARCH REPORT

Inter: nal Application No

PCT/GB 00/00644

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61N5/10 G21G4/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61N G21G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 994 013 A (SUTHANTHIRAN KRISHNAN ET AL) 19 February 1991 (1991-02-19) the whole document	1,2,4-6, 8-11,13
Y	—	7,12,14
Y	US 4 550 100 A (HOFMEISTER HELMUT ET AL) 29 October 1985 (1985-10-29) column 2, line 16 - line 24 column 3, line 32 - line 59	7,12
Y	US 5 199 939 A (DAKE MICHAEL D ET AL) 6 April 1993 (1993-04-06) abstract	14
A	US 5 342 283 A (GOOD ROGER R) 30 August 1994 (1994-08-30) column 4, line 10 - line 15 column 6, line 3 - line 21	3-6,15
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *g* document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/GB 00/00644

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 98 19713 A (STS BIOPOLYMERS INC ;VIOLANTE MICHAEL R PH D (US); LYDON MARGARET) 14 May 1998 (1998-05-14) page 2, line 28 -page 3, line 24</p>	3,15

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Information on patent family members

International Application No

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			CN 1236322 A	24-11-1999
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- (71) Applicant (for all designated States except US): NYCOMED AMERSHAM PLC [GB/GB]; Amersham Laboratories Building, 21 White Lion Road, Amersham, Buckinghamshire HP7 9LL (GB).
- (72) Inventors; and
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- (81) Designated States (national): AE, AL, AM, AT, AT (utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ (utility model), DE, DE (utility model), DK, DK (utility model), DM, EE, EE (utility model), ES, FI, FI (utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR (utility model), KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (utility model), SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
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- Published:
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IODINE-CONTAINING RADIOACTIVE SOURCES

(57) Abstract: A radioactive source for use in brachytherapy comprising a radioactive isotope of iodine in the form of iodide ions or an iodine-containing compound adsorbed on the surface of a substantially non-radiation attenuating substrate. Preferably the source is a seed and the radioisotope is iodine-125. Preferred substrates include carbon, particularly activated carbon. The sources may be useful for the treatment of restenosis.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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INTERNATIONAL SEARCH REPORT

Inter. Application No

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